

Claims

1. Agent for inhibiting development or progress of proliferative diseases
5 and especially cancer diseases or of other diseases which are accompanied by elevated PLK1 expression levels, characterized in that it reduces or inhibits the activity of polo like kinase 1 (PLK1) in mammalian cells.
- 10 2. Agent according to claim 1, characterized in that it contains at least one short interfering RNA (siRNA) or antisense RNA which is directed against the PLK1 gene as active agent.
3. Agent according to claim 2, characterized in that the RNA comprises
15 15 to 30 nucleotides.
4. Agent according to claims 2 or 3, characterized in that the sequence of the dsRNA or antisense RNA corresponds to nucleotide sequences of the PLK1 mRNA.
- 20 5. Agent according to claim 4, characterized in that the dsRNA corresponds to positions 178-200 (siRNA2), 362-384 (siRNA3), 1416-1438 (siRNA4) or 1570-1592 (siRNA5) of the PLK1 gene.
- 25 6. Agent according to anyone of claims 1 to 5, comprising an effective amount of
 - 1) at least one RNA expression system and optionally
 - 2) a nuclease inhibiting substance,wherein said RNA expression system contains
 - a) at least one RNA polymerase specific promoter sequence and is
30 under the transcriptional control of said promoter sequence

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b) at least one genetic information homologous to the PLK1 gene, wherein said genetic information under suitable conditions and in the presence of an RNA polymerase is transcribed into interfering RNA.

- 5 7. Agent according to claim 6, wherein said interfering RNA is a siRNA, preferably a shRNA (hairpin) or a short antisense RNA.
8. Agent according to claim 6 or 7, wherein said RNA expression system is contained in a plasmid or viral vector.
- 10 9. Agent according to anyone of claims 6 to 8, wherein the genetic information comprises two complementary and inverted sequences (hairpin) which are homologous to the PLK1 gene.
- 15 10. Agent according to claim 9, wherein each of said two sequences is 15 to 30 nucleotides long.
11. Agent according to claims 9 or 10, wherein said sequences are connected by a spacer sequence.
- 20 12. Agent according to claim 11, wherein the spacer sequence contains 3 to 10 nucleotides.
- 25 13. Agent according to anyone of claims 6 to 12, wherein the genetic information b) contains an RNA polymerase stop signal at the 3' end.
14. Agent according to anyone of claims 6 to 13, wherein the nuclease inhibitor is aurin tricarboxylic acid (ATA).
- 30 15. Agent according to anyone of claims 6 to 14, wherein the RNA specific promoter is the U6 promoter or H1 promoter.

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16. Agent according to anyone of claims 6 to 15, wherein it is formulated for intravenous administrations.
- 5 17. Agent according to claim 16, wherein it is formulated for bolus injection.
18. Agent according to claims 16 or 17, wherein the active substances are contained in buffered saline solution.
- 10 19. Agent according to anyone of claims 6 to 19, wherein the expression system is contained in an amount suitable for delivery of 0.05 to 0.5 mg/kg body weight of a patient.
- 15 20. Agent according to claim 1, characterized in that it contains at least one phosphorothiate antisense oligonucleotide (ASO) or an ASO with another modification like mixed backbone oligonucleotides or morpholino oligonucleotides directed against the PLK1 gene as active agent.
- 20 21. Agent according to claim 20, characterized in that the ASO contains 15 to 30 nucleotides.
22. Agent according to claims 20 or 21, characterized in that the ASO is homologous to the PLK1 mRNA.
- 25 23. Agent according to claim 22, characterized in that the ASO is P12 and/or P13.
24. Agent according to claim 1, characterized in that a peptide which is inhibitory for the PLK1 gene is present as active agent.
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25. Agent according to claim 24, characterized in that the peptide comprises 3 to 50 amino acids.

5 26. Agent according to claims 24 or 25, characterized in that the peptide corresponds to a wild type (aa 410-439 in PLK1) or a mutated polo box or its polo-box similar structures in PLK1-3.

10 27. Agent according to anyone of claims 24 to 26, characterized in that the peptide corresponds to the polo box or the mutated polo box with any modifications, like L-forward, L-reverse, D-reverse (retro-inverso), sidechain and backbone modifications, cyclic forms and repeats as well as other modifications which enhance the half-life of peptides.

15 28. Agent according to anyone of claims 24 to 27, characterized in that the peptide is linked to a protein transduction domain or is used together with a protein transduction domain without need for a chemical covalent coupling or other expression-vector systems (plasmids, viral vectors etc.).

20 29. Agent according to anyone of claims 24 to 28, characterized in that it contains peptide P1 and/or peptide P2.

25 30. Pharmaceutical composition, characterized by containing an effective amount of an agent according to anyone of claims 1 to 29, optionally together with useful auxiliary and/or carrier substances and /or inhibitors of proteinases.

30 31. Method for treating patients who suffer from proliferative disease and especially cancer disease, characterized by administration of an effective amount of an agent according to anyone of claims 1 to 29 or of a pharmaceutical composition according to claim 30.